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THE VETERINARY JOURNAL

A MONTHLY REVIEW OF VETERINARY SCIENCE

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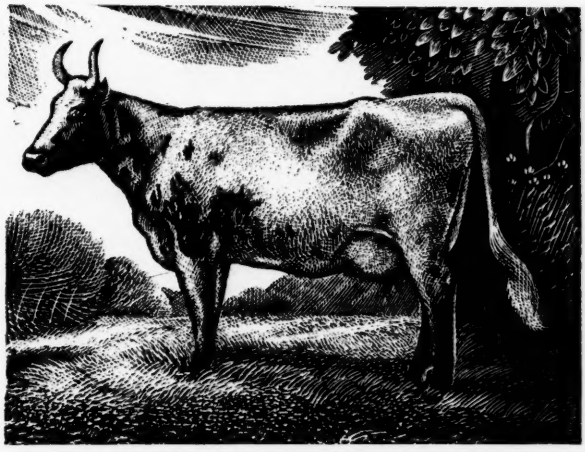

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THE VETERINARY JOURNAL

EDITORS: T. DALLING, *M.A., M.R.C.V.S.* J. McCUNN, *M.R.C.V.S., L.R.C.P.*

Vol. 103 June, 1947 No. 6

EDITORIAL

SULPHONAMIDE THERAPY

EFFECTIVE antibacterial chemotherapy has been achieved during the last decade and there can be little doubt that it will rank in medical history with the period when Lister introduced antiseptic surgery.

Thousands of drugs related to sulphanilamide have been synthesised and tested experimentally in laboratory animals and those with promise tested in man. Usually only those which have been successful in man, not more than ten main types, have been tried in the domestic animals, and there has often been a tacit assumption that their relative behaviour and clinical value would be similar in man and the domestic animals. This is only true in the broadest sense because the invading bacteria differ in the various species as do the absorption, excretion and metabolism of the different drugs.

The potent drugs now available can only be used effectively when we know the blood-levels they produce and their antibacterial potency against the various specific bacteria. Drugs are sometimes transferred from use in human to veterinary medicine without this basic information being obtained.

We publish an article in this issue which, together with that published elsewhere[1], provide some of the information on pharmacology and antibacterial potency necessary for the proper use of the sulphonamide drugs. In addition, these articles show how important it is that pharmacological (or physiological) studies should be carried out in the domestic animals, because it has been shown that sulphadiazine, which produces the best, or almost the best, blood-levels in man and mouse, produces relatively low levels in the farm animals. In addition, it has been shown that 4:4'diaminodiphenyl-sulphone, which produces methæmoglobinæmia in laboratory animals and man, is free from this defect in cattle and sheep. It is less toxic than sulphanilamide for cattle, but produces toxic nervous symptoms in sheep. It is the most potent of the sulphonamide drugs against *Str. agalactiæ* and the most persistent when injected into the cow's udder, and may, therefore, be of special value in the treatment of mastitis, particularly in combination with penicillin. In this form it produced bacteriological cure of *Str. agalactiæ* infection in 94.4 per cent. of 54 quarters treated with a single injection[1], whereas it appears that not more than 60 per cent. of cures are

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obtained with a single injection of penicillin, however large the dose. The results obtained with sulphone/penicillin obviously require confirmation.

Pneumonic and enteric infections in young animals are largely associated with Gram-negative organisms, and against these 4 :4'diaminodiphenyl-sulphone is relatively much less potent than against streptococci. Sulphathiazole, sulphamezathine, sulphamerazine and sulphadiazine are all more potent antibacterial drugs than sulphapyridine. From a consideration of these facts and their pharmacology it was concluded[1] that for the treatment of pneumonia in cattle, sheep and pigs, sulphamezathine and sulphamerazine would probably be the most effective drugs, although sulphathiazole might be the most active if given frequently and in large doses. Sulphamezathine appeared specially suitable for the pig. Jones (1947) treated 95 cases of calf pneumonia from 1942 to 1944. The cases were randomised and 68.2 per cent. of the untreated animals died, 25 per cent. of those treated with sulphapyridine, 20.8 per cent. with sulphadiazine and 16.0 per cent. with sulphathiazole. He recommends a dose of approximately 0.2 gm./kilo. of sulphathiazole for two to three days, followed by a dose of 0.1 gm./kilo. for another two or three days unless recovery has occurred. With sulphadiazine and sulphapyridine only half the above doses are given. These are similar to the doses recommended by Francis, and it is important to note that particularly with the more persistent drugs such as sulphamezathine and sulphamerazine in calves, and sulphamezathine in pigs, the animals need only be dosed once daily. Both Jones (1947) and Thorp (1945) concluded that sulphathiazole acted more quickly than sulphadiazine or sulphamerazine in calf pneumonia. There can be no doubt that sulphaguanidine is contra-indicated for treating the enteric diseases of animals, because other drugs are more effective. There may be little to choose between the value of sulphamezathine, sulphamerazine, sulphadiazine or sulphathiazole in these conditions.

Now that a considerable amount of basic information is available, it would seem that adequate trials should be carried out in Great Britain to find the optimum doses and compare the efficiency of sulphathiazole, sulphamezathine, sulphamerazine and perhaps sulphadiazine for the treatment of enteric and pneumonic infections in young animals with that of sulphapyridine, which has so far been largely employed in these conditions. If precise information could be obtained, it would do much to reduce the confusion which has been produced in the minds of practitioners by conflicting claims not always based on adequate evidence.

REFERENCES

1. Francis, J., 1947: "Bacterial Chemotherapy in Veterinary Medicine," *Vet. Rec., 59,* 131-137.

Jones, L. Meyer, 1947: "The Use of Sulfathiazole, Sulfapyridine and Sulfadiazine in the Treatment of Calf Pneumonia," *Amer. J. Vet. Res., 8,* 14-28.

Thorp, W. T. S., 1945: "The Newer Sulphonamides in Veterinary Practice," *J. Amer. Vet. Med. Ass., 106,* 75-81.

GENERAL ARTICLES

SOME OBSERVATIONS ON THE PHARMACOLOGY OF THE SULPHONAMIDES AND 4:4′ DIAMINO-DIPHENYL SULPHONE* IN THE DOMESTIC ANIMALS

By JOHN FRANCIS, B.Sc., M.R.C.V.S.

Imperial Chemical Industries Limited, Biological Laboratories, Wilmslow, Cheshire

FOLLOWING the administration of a single oral dose of the sulphonamides the blood-level produced can be plotted against time and the area enclosed by the curve may be termed the blood-level curve area (B.L.C.A.). The average relative blood-level curve areas in the calf, sheep, pig, and horse produced by the common sulphonamides and by sulphone have been determined by Francis (1947) and are shown below when sulphanilamide is given a value of unity:—

Sulphanilamide	1.0
Sulphathiazole	0.27
Sulphapyridine	0.68
Sulphadiazine	0.58
Sulphamerazine	1.98
Sulphamezathine	1.81
Sulphone	2.93

In this paper observations on the blood-levels produced by repeated doses of the sulphonamides, when given in various ways, and their behaviour when injected into the udder are described.

In man the sulphonamides are often administered every four or six hours, but dosing even at eight-hourly intervals is difficult in animals and it will be seen from the blood-level curves (Francis, 1947) that it is certainly not necessary in the calf or sheep and probably not in the pig or horse. At first we were chiefly interested in the behaviour of sulphone and sulphamezathine in the calf and sheep and as both these drugs produce persistent blood-levels we adopted a standard dosing schedule of 0.1 gm./kilo., followed by half this dose once daily.

Calves

It can be seen from Tables I and IV that an initial dose of 0.1 gm./kilo. of sulphone followed by half this dose on the four subsequent mornings produced average morning levels of 4.61 mgs. per cent. and evening levels of 5.23 mgs. per cent. in five young calves, i.e., an almost constant blood-level of about 5 mgs. per cent. In a smaller series of experiments with the compound "364" (4:4′ nitro-amino diphenyl sulphone) similar results were obtained. In addition, calf 39, weighing 36 kilos., was given a daily dose of 0.1 gm./kilo. for one week, 0.2 for the next and 0.3 for the third week. Two doses of 0.4 gm./kilo. at the end of the third week produced slight nervous symptoms. The average blood-level during the first week was 3.8 mgs. per cent., during the second 5.9 mgs. per cent., and the third 8.9 mgs. per cent. Following the two larger doses in the fourth week the level rose to a maximum of 14.2 mgs. per cent. During all this time the calf showed no ill-effect except for slight nervous symptoms (nodding of the head) during the day that the maximum blood-level was reached. By the end of the

* Henceforth called sulphone.

dosing period the calf's weight had increased to 45 kilos. and Table II shows that up to the third week there had only been a slight drop in the percentage of hæmoglobin and an increase in the number of white cells. After the fourth week the hæmoglobin level fell to 60 per cent., but there was no other change.

Calf 1, weighing 190 kilos., was given a dose of 0.3 gm./kilo. on eleven successive mornings, producing an average morning blood-level of 11.25 mgs. per cent., and evening level of 13 mgs. per cent. By the tenth day the weight of the calf had fallen to 133 kilos. and the number of white cells had been halved, but ten days later the weight had increased to 190 kilos., and it continued to gain in weight. At the end of the dosing period the fæcal level was 120 mgs. per cent. The urine was cloudy and contained 320 mgs. per cent. of the free drug and 1,300 mgs. per cent. of the acetylated drug.

TABLE I

BLOOD-LEVELS PRODUCED BY THE ADMINISTRATION OF REPEATED DOSES OF SULPHONE AND "364" TO CALVES.

CALF NO.	WT. IN KILOS.	DRUG	NO. DAYS DOSED	DOSE GMS./KILO		BLOOD-LEVEL MGS.% A.M.	BLOOD-LEVEL MGS.% P.M.	FAECAL LEVEL MGS.%
51	39.0	Sulphone	6	0.1 followed by 0.05 once daily	Max.	8.0	8.4	
					Min.	5.2	8.0	
					Aver.	7.0	8.25	66 (1)
41	205.0	"	5	Ditto	Max.	5.0	6.2	
					Min.	3.0	4.0	
					Aver.	3.98	4.64	11 (1)
53	43.7	"	5	Ditto	Max.	6.0	6.0	
					Min.	4.0	4.0	
					Aver.	4.48	5.08	24 (1)
60	39.5	"	5	Ditto	Max.	4.6	8.0	
					Min.	1.0	3.6	
					Aver.	3.0	3.36	
42	30.9	"	5	Ditto	Max.	4.2	4.6	
					Min.	3.2	2.2	28.7
					Aver.	5.65	4.35	(3)
1	190	"	11	0.3 daily	Max.	15.0	16.0	
					Min.	9.6	12.0	
					Aver.	11.25	13.0	
39	38.3	"	1st week	0.1 daily	Max.	4.2	6.0	
					Min.	2.0	2.0	
					Aver.	3.2	4.4	52 (1)
		"	2nd week	0.2 daily	Max.	6.4	8.8	
					Min.	2.0	5.0	
					Aver.	5.06	7.1	48 (1)
		"	3rd week	0.3 daily	Max.	10.4	12.4	
					Min.	5.6	5.6	
					Aver.	8.7	9.2	84 (1)
31	140	"364"	4	0.1 followed by 0.05 once daily	Max.	4.4	4.0	
					Min.	2.6	0.8	
					Aver.	3.35	3.2	
34	130	"	4	0.1 daily	Max.	6.0	6.8	
					Min.	3.8	2.6	
					Aver.	4.9	4.55	

Figures in brackets show the number of fæcal samples examined.

Subsequently we gave an initial dose of 0.1 gm./kilo. of the common sulphonamides followed by half this dose on four successive mornings to groups of three or four calves. The results are shown in Table III and are summarised in Table IV.

The differences between the various drugs were less than those obtained following the administration of single doses, but the same relative order was maintained. Sulphamezathine, sulphamerazine, sulphone and "364" (4 : 4′ nitro-amino diphenyl sulphone) produced average daily blood-levels of four to five mgs. per cent., sulphanilamide, sulphapyridine and sulphadiazine about 2-3 mgs. per cent., and sulphathiazole only 1 mg. per cent. Determination of fæcal levels was carried out on 16 calves receiving 0.1 followed by 0.05 gm./kilo. and the results are shown in Tables I and III. There seems to be no significant difference between the levels produced by the various drugs; the average level was 33 mgs. per cent.

Sheep

Sheep 33 and 35 were given an initial dose of 0.1 gm./kilo. of sulphone followed by 0.03 gm./kilo. as a single dose each morning for seven days (Table V).

Blood samples were taken at 9.30 every morning before dosing and again at 4.30 in the afternoon. The results in the two sheep were similar; the respective average morning levels were 2.5 and 3.01 mgs. per cent., and evening levels 3.2 and 3.36

TABLE II

CHANGES IN THE COMPOSITION OF THE BLOOD IN CATTLE GIVEN VARIOUS DOSES OF SULPHONE

CALF NO.	DAY	HAEM %	RED CELLS THOUSANDS	WHITE CELLS	DIFFERENTIAL COUNT, PER CENT.				
					LYMPHS	MONOS	POLYS	EOSINS	BASOS
39[1]	0	92	9,510	5,750	63	10	27	0	0
	7	92	9,710	8,300	68	6	21	1	0
	14	90	9,670	10,600	66	2	32	0	0
	21	85	9,100	14,800	75	5	20	0	0
	24	80	9,310	12,900	78	2	20	0	0
	28	60	8,510	12,750	72	4	23	1	0
1[1]	0	65	7,380	14,750	55	6	39	0	0
	7	67	8,140	16,800	39	1	60	0	0
	14	60	7,420	6,300	64	5	31	0	0
16[2] (Cow)	0	74	6,200	7,440	59	6	27	8	0
	8	72	6,100	8,230	30	3	64	3	0

[1] See Table I for dose and blood-levels.
[2] See Table XII for dose and blood-levels.

mgs. per cent. At the end of the period one sheep had a fæcal level of 20 mgs. per cent. and the other of 32 mgs. per cent. In both sheep there was some decrease in the number of polymorphonuclear leucocytes (Table VI), but there was no other significant change in the blood and no toxic symptoms were observed.

TABLE III

BLOOD-LEVELS (MGS.%) IN CALVES PRODUCED BY VARIOUS DRUGS GIVEN AT AN INITIAL DOSE OF 0.1 GMS./KILO. FOLLOWED BY FOUR MORE DOSES OF 0.05 GMS./KILO. ONCE DAILY.

DRUG		A.M.	P.M.	FAECAL	A.M.	P.M.	FAECAL	A.M.	P.M.	FAECAL
		CALF 52 38.6 KILOS.			CALF 55 33.6 KILOS.			CALF 90 47.2 KILOS.		
Sulphanilamide	Max.	2.2	4.6		1.6	4.5		3.6	4.0	
	Min.	1.4	0.7		0.6	1.4		1.2	3.0	
	Aver.	1.92	2.86	70	1.06	2.92		2.24	3.72	15
		CALF 51 40.0 KILOS.			CALF 56 33.6 KILOS.			CALF 57 56.3 KILOS.		
Sulphathiazole	Max.	1.2	2.0		1.8	4.4		0.5	1.1	
	Min.	1.0	0.2		0	1.0		0	0.9	
	Aver.	1.14	1.42	30	0.64	2.02		0.24	1.0	
		CALF 54 36.3 KILOS.			CALF 55 40.0 KILOS.			CALF 58 55.4 KILOS.		
Sulphapyridine	Max.	4.3	6.0		2.4	4.6		1.4	1.8	
	Min.	1.4	2.4		1.0	2.4		0.6	1.0	
	Aver.	2.78	3.8		1.44	2.72	30	1.04	1.36	
		CALF 53 36.3 KILOS.			CALF 56 37.1 KILOS.			CALF 87 44.09 KILOS.		
Sulphadiazine	Max.	4.2	4.4		2.0	2.4		4.2	4.8	
	Min.	2.4	3.6		1.2	1.8		2.4	2.2	
	Aver.	3.64	4.1	36	1.5	2.28	34	3.2	2.96	20
		CALF 80 82.7 KILOS.			CALF 100 35.4 KILOS.			CALF 59 33.6 KILOS.		
Sulphamerazine	Max.	3.8	4.6		4.4	6.4		2.4	4.2	
	Min.	2.2	2.8		3.0	3.5		1.0	3.0	
	Aver.	2.88	4.0	15	3.6	4.7	28	1.84	3.48	
		CALF 52 38.1 KILOS.			CALF 54 39.0 KILOS.			CALF 90 37.2 KILOS.		
Sulphamerathine	Max.	6.2	9.4		4.6	6.0		4.2	6.6	
	Min.	4.2	7.4		3.2	2.8		2.0	4.2	
	Aver.	5.48	8.45	46	3.92	4.72	56	3.08	5.2	24

Figures for the fæcal level represent the results of one determination on the fourth day.

Sheep 31 and 36 were given a daily dose of 0.1 gm./kilo. of sulphone for four days (Table V); the blood-levels rose to 6 mgs. per cent. in one sheep, and 8.0 in the other, and although no toxic symptoms were observed the dose was reduced to 0.05 gm./kilo. for another four days, but the blood-levels remained high and the dose was again halved. Dosing was continued for a total period of three weeks, the average daily dose being 0.045 gm./kilo. The average morning levels of the two sheep (just before dosing) were 3.54 and 3.3 mgs. per cent. and the evening levels 4.2 and 4.0 mgs. per cent. The average fæcal

TABLE IV.

AVERAGE BLOOD-LEVELS (MGS.%) IN CALVES PRODUCED BY THE ORAL ADMINISTRATION OF AN INITIAL DOSE OF 0.1 GM./KILO. FOLLOWED BY HALF THIS DOSE ONCE DAILY FOR FOUR DAYS

DRUG	NO. CALVES	A.M.	P.M.	DAILY
Sulphanilamide	3	1.74	3.17	2.45
Sulphathiazole	3	0.67	1.48	1.07
Sulphapyridine	3	1.41	2.62	2.01
Sulphadiazine	3	2.78	3.11	2.94
Sulphamerazine	3	2.77	4.06	3.41
Sulphamezathine	3	4.12	6.12	5.12
Sulphone	5	4.61	5	4.97
M.364	2	4.12	3.87	3.99

TABLE V

BLOOD AND FÆCAL LEVELS (MGS.%) PRODUCED BY REPEATED DOSES OF VARIOUS SULPHONAMIDES IN SHEEP.

SHEEP NO.	WT. KILO.	DRUG	DAYS DOSED	DOSE		A.M.	NOON	P.M.	FÆCAL LEVEL
12	59.0	Sulphamezathine	4	0.2 gm. then 0.1 twice daily	Max.	11.6	23.4	17.6	
					Min.	5.4	8.0	6.0	
					Aver.	7.98	13.6	10.65	
13	52.7	Sulphanilamide	4	0.2 gms. then 0.1 twice daily	Max.	18.0	22.0	16.6	
					Min.	10.2	12.0	12.0	
					Aver.	12.5	17.9	14.15	
33	53.6	Sulphone	8	0.1 gms. then 0.05 once daily	Max.	3.4		4.0	
					Min.	1.6		2.4	
					Aver.	2.5		3.2	20 (1)
35	51.8	"	8	0.1 gms. then 0.05 once daily	Max.	4.5		4.4	
					Min.	2.0		2.2	
					Aver.	3.01		3.36	32 (1)
31	50.9	"	22	Average of 0.045 gm.	Max.	5.4		8.0	76
					Min.	1.8		2.3	26
					Aver.	3.54		4.2	48 (8)
36	50.9	"	22	Average of 0.045 gm.	Max.	5.4		6.0	88
					Min.	2.2		2.6	28
					Aver.	3.3		4.0	50 (6)

Figures in brackets show the number of fæcal samples examined.

TABLE VI

CHANGES IN THE COMPOSITION OF THE BLOOD IN SHEEP GIVEN VARIOUS DOSES OF SULPHONE*

NO.	DAY	HAEM. %	RED CELLS THOUSANDS	WHITE CELLS	DIFFERENTIAL COUNT PER CENT.					DAY	HAEM. %	RED CELLS THOUSANDS	WHITE CELLS	DIFFERENTIAL COUNT PER CENT.				
					LYMPHS	MONOS	EOSINS	POLYS	BASOS					LYMPHS	MONOS	EOSINS	POLYS	BASOS
12	1	82	9,170	8,900	45	4	4	47	0	6	77	9,420	7,200	57	1	9	32	0
13	1	83	9,850	9,900	53	3	4	30	0	6	76	8,520	15,000	40	3	0	57	0
33	1	85	9,740	12,950	65	5	10	20	0	10	83	10,590	10,950	67	5	19	9	0
35	1	82	9,480	11,850	45	8	8	38	1	10	76	10,310	8,000	75	5	13	7	0
31	1	88	11,520	6,700	70	2	13	15	0	22	70	8,100	9,600	79	3	18	0	0
36	1	74	9,480	8,750	59	7	10	24	0	22	74	10,070	7,600	83	3	0	14	0

* See Table V for details of dosing and blood-levels.

TABLE VII

BLOOD-LEVELS IN PIGS PRODUCED BY THE SUBCUTANEOUS INOCULATION OF 0.1 GM./KILO. OF SODIUM SULPHAMEZATHINE AND SULPHONE E.O.S.

DRUG	PIG	WT. KILO.	TIME IN HOURS 1	2	3	5	7	24	32
			MGS. % IN BLOOD						
Sodium sulphamezathine	1	40.0	9.6	12.8	12.4	11.6	10.0	5.2	2.6
	2	53.6	6.0	8.0	7.2	7.2	6.2	3.2	3.2
	3	58.1	12.4	12.4	11.6	10.4	10.0	5.2	4.6
Average			9.33	11.0	10.4	9.73	8.4	4.53	3.47
Sulphone E.O.S.	5	55.0	10.2	10.2	7.6	4.0	3.0	1.6	1.6
	6	41.8	11.2	10.0	6.6	3.8	3.8	1.8	1.8
Average			10.7	10.1	7.1	3.9	3.4	1.7	1.7

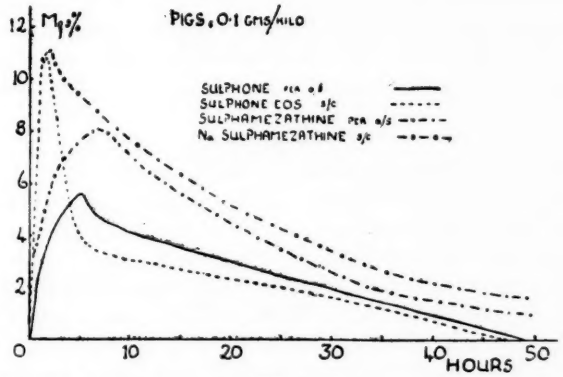

Fig. 1
Blood-levels produced following the oral and subcutaneous administration of sulphone and sulphamezathine to pigs.

TABLE VIII

BLOOD-LEVELS (MGS.%) IN PIGS PRODUCED BY FIVE ORAL DOSES OF 0.1 GM./KILO. OF SULPHONE AND SULPHAMEZATHINE* GIVEN ONCE DAILY.

DRUG		A.M.	P.M.	FAECAL	A.M.	P.M.	FAECAL	A.M.	P.M.	FAECAL
		PIG 1, 40.0 KILO.			PIG 6,41.8 KILO.			PIG 2,53.6 KILO.		
Sulphamezathine	Max.	7.2	12.0		7.4	12.0		6.2	10.4	
	Min.	5.2	7.2		6.0	7.4		4.4	7.2	
	Aver.	6.28	8.92	55.0	6.56	10.04	48.0	5.2	9.2	47.0
		PIG 3,58.1 KILO.			PIG 4,55.0 KILO.			PIG 5,55.0 KILO.		
Sulphone	Max.	4.6	9.0		4.8	8.0		5.0	8.0	
	Min.	3.0	6.0		3.6	5.4		3.8	6.0	
	Aver.	3.92	7.28	28.0	4.2	7.28	29.0	4.48	7.04	28.0

In each instance the fæcal-levels given represent the average of two analyses.
* See Table V for details of dosing and blood-levels.

* See Table V for details of dosing and blood-levels.

XUM

levels were 48 and 50 mgs. per cent. In sheep 31 there was a drop in the percentage of polymorphonuclear leucocytes, in hæmoglobin, and in the number of red cells, but no toxic symptoms were observed at any time (Table VI).

Sheep 12 and 13 (Table V) were given an initial dose of 0.2 gm./kilo. of sulphamezathine and sulphanilamide respectively on the evening of one day, followed by 0.1 gm./kilo. morning and evening for four more days. Blood samples were taken morning and evenings, immediately before dosing, and at mid-day. Both drugs produced high blood-levels, but it is interesting to note that at each time interval the level produced by sulphanilamide was higher than with sulphamezathine. The average sulphanilamide level was 14.9 mgs. per cent. and the sulphamezathine level 10.4 mgs. per cent. The difference between morning and evening levels was also greater with sulphamezathine than with sulphanilamide. These findings therefore corroborate those obtained when single doses of these drugs were given to sheep (Francis, 1947). Hæmoglobin estimations and blood counts were carried out every day; no significant changes occurred (Table VI).

Four days after dosing had ceased sheep 13, which had received sulphanilamide, developed anorexia, ataxia of the hind limbs and a temperature of 104.5 deg. F. The following day there was slight improvement, but the temperature was 105 deg. F. Two days later the sheep walked normally and its appetite was improving.

Pigs

Pigs are the only animals examined in which sulphone was not the most persistent drug (Francis, 1947); in this species its place was taken by sulphamezathine, and further experiments were carried out with these two drugs. If a pig will not eat, the most satisfactory way of giving it a drug is by injection. Sodium sulphamezathine and sulphone E.O.S. were, therefore, given subcutaneously at doses of 0.1 gm./kilo. It can be seen from Table VII and Fig. 1 that sulphamezathine produced a blood-level rising to a maximum of 11 mgs. per cent. after two to three hours which did not fall below 2 mgs. per cent. until about 48 hours after dosing. Sulphone E.O.S. produced about the same maximum blood-level, which fell rapidly until the seventh hour and then much more slowly. This is similar to the results obtained by Rose (1945) with mice, and is, no doubt, due to the fact that sulphone E.O.S. is rapidly excreted; any drug remaining in the body after seven hours is in the form of sulphone and is then excreted slowly.

Groups of three pigs were fed 0.1 gm./kilo. of sulphamezathine and 0.1 gm./kilo. of sulphone in their mash once daily. The results are shown in Table VIII and it will be seen that the following average levels were obtained during the period of dosing:—

	7 hours after each dose		24 hours after each dose
Sulphamezathine ...	9.45 mgs. per cent.	...	6.0 mgs. per cent.
Sulphone	7.32 mgs. per cent.	...	4.2 mgs. per cent.

Sulphone produced no nervous symptoms in any of the pigs, but unfortunately quite severe methæmoglobinæmia developed.

Horses

Sulphone was by far the most persistent drug, but unfortunately produced severe methæmoglobinæmia in this species; sulphamezathine was slightly more per-

TABLE IX

BLOOD-LEVELS IN HORSES PRODUCED BY THE INTRAPERITONEAL INOCULATION OF 0.1 GM./KILO. OF SODIUM SULPHAMEZATHINE

HORSE	WT. KILO.	TIME IN HOURS							
		1/3	2/3	1	2	3	5	7	24
		BLOOD-LEVELS MGS.%							
8	500	2.2	3.8	6.0	5.2	4.8	4.2	3.8	1.4
10	490	12.2	13.6	16.0	14.0	12.2	8.0	8.0	2.6
12	470	13.6	14.0	14.0	15.2	12.0	7.2	6.8	3.8
Average		9.33	10.47	12.0	11.47	9.7	6.47	6.2	2.6

TABLE X

BLOOD-LEVELS IN HORSES PRODUCED BY A TOTAL DAILY DOSE OF 0.15 GM./KILO. SODIUM SULPHAMEZATHINE GIVEN I/P.

0.05 GM./KILO. A.M. 0.1 " P.M.					0.15 GM./KILO. P.M.			
HORSE	WT. KILO.	BLOOD-LEVELS MGS.%			HORSE	WT. KILO.	BLOOD-LEVELS MGS.%	
			a.m.	p.m.				a.m. p.m.
8	500	Max.	9.0	7.6	11	410	Max.	11.2 9.0
		Min.	3.2	3.4			Min.	5.2 3.6
		Aver.	6.1	5.15			Aver.	7.75 6.1
10	490	Max.	8.0	10.2	12	470	Max.	9.0 6.4
		Min.	4.0	5.2			Min.	4.6 2.4
		Aver.	6.2	7.5			Aver.	6.75 5.3
Total Average 6.21								6.47

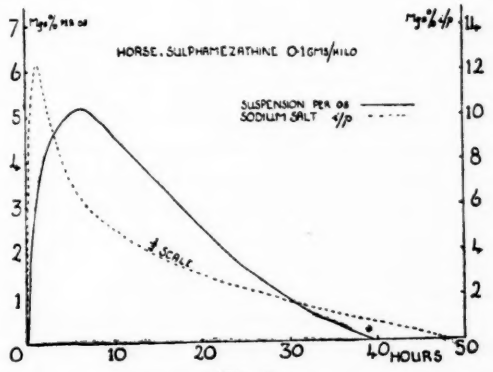

Fig. 2
Blood-levels produced following the oral and intraperitoneal administration of sulphamezathine to horses.

sistent than sulphamerazine or sulphadiazine (Francis, 1947). Oral administration may be difficult in the horse and it would be valuable if there were a drug which could be injected in large quantities. Although the sodium salt of sulphamezathine is less irritant than that of the other sulphonamides, doses of 150-200 c.c. of a 33.3 per cent. solution cannot be given subcutaneously. Intravenous injection is not always easy to perform as a routine in practice, so we gave a dose of 0.1 gm./kilo. intraperitoneally to three horses. The injection was carried out halfway between the last rib and the crest of the ilium without difficulty and without any untoward effect. The blood-levels are shown in Table IX, and although they were much lower in one horse than in the other two, the average B.L.C.A. was considerably larger than following oral dosing (Fig. 2).

Two horses were given a dose of 0.15 gm./kilo. once daily for four days and two a dose of 0.1 gm./kilo. each evening and 0.05 gm./kilo. in the morning. When these injections were being made it was found that unless the solution was warmed the horse might show evidence of slight abdominal pain following injection. Whether the sodium salts of sulphamerazine and sulphadiazine would be as satisfactory as sodium sulphamezathine for intraperitoneal injection is not known. The blood-levels produced by these repeated intraperitoneal injections are shown in Table X, and it will be seen that the average was 6.2 and 6.47 mgs. per cent. in the two pairs of horses. There was very little difference between the morning and evening levels, but it should be remembered that the main dose was given in the evening and samples taken after 16 and 24 hours; there was almost certainly a peak of 10-12 mgs. per cent. three to four hours after dosing.

Cows

The blood- and milk-levels produced by single oral doses of sulphanilamide and sulphone have been described (Francis, 1947). Three cows were given a dose of 60 gms. sulphone on three successive mornings. The following week they were given an initial dose of 90 gms. of sulphanilamide, followed by two doses of 30 gms. later that day, and three doses of 30 gms. on the two successive days. The results are shown in Table XI and the following average levels were obtained over the period of dosing:—

		Sulphanilamide	Sulphone
Blood	a.m.	6.71 ...	4.17
	p.m.	8.42 ...	7.85
Milk	a.m.	8.47 ...	1.48
	p.m.	10.49 ...	2.11

In these two series of experiments the difference in the toxicity of sulphone and sulphanilamide was very noticeable. During treatment with sulphone the cows were normal, but as soon as sulphanilamide was given they began to scour, developed severe anorexia, and the milk yield dropped. Berger (1945) has also noted that in quite a large proportion cows, and in almost every cow in some herds, sulphanilamide produced this effect. A few of the same cows treated with sulphone have shown no toxic effects.

Cow 16 was dosed orally with sulphone on eight successive days. On the first two days she received 0.3 gm./kilo. (approx. 120 gms.) and on subsequent days 0.2 gm./kilo. Blood-levels were taken morning and evening, as were for milk samples from each quarter, and a sample bulk milk. All the milk samples taken

TABLE XI

BLOOD AND MILK-LEVELS PRODUCED BY AN INITIAL DOSE OF 90 GRAMMES OF SULPHANILAMIDE FOLLOWED BY 30 GRAMMES THREE TIMES DAILY FOR THREE DAYS, AND THREE SINGLE DAILY-DOSES OF 60 GRAMMES OF SULPHONE

BLOOD-LEVELS MGS.%				MILK-LEVELS MGS.%			
SULPHANILAMIDE		SULPHONE		SULPHANILAMIDE		SULPHONE	
A.M.	P.M.	A.M.	P.M.	A.M.	P.M.	A.M.	P.M.
	8.4		8.0		14		1.8
6.0	8.4	3.8	9.0	10.2	12.6	1.4	3.2
8.4	8.4	4.8	9.8	8.2	10.4	1.8	2.6
8.0		5.6		10.0		1.5	
7.47	8.4	4.73	8.93	9.47	12.33	1.57	2.53
	7.4		5.6		10		1.5
6.2	9.0	2.4	6.6	8.2	8.2	1.4	1.5
6.0	8.4	4.2	8.0	8.2	8.4	1.6	1.8
6.4		4.0		6.4		1.2	
6.2	8.26	3.53	6.7	7.6	8.87	1.4	1.6
	9.4		7.0		13.2		1.8
6.4	8.4	3.6	7.0	9.4	9.4	1.6	2.4
7.0	8.0	4.6	9.8	9.4	8.2	1.8	2.4
6.0		4.6		6.2		1.0	
6.47	8.6	4.27	7.93	8.33	10.27	1.47	2.2
AVERAGE - ALL COWS							
6.71	8.42	4.17	7.85	8.47	10.49	1.48	2.11

TABLE XII

BLOOD-LEVELS IN COW 16 PRODUCED BY REPEATED DOSES OF SULPHONE.

DAY	DOSE GM./KILO. P.M.	BLOOD-LEVELS MGS.% A.M.	BLOOD-LEVELS MGS.% P.M.	BULK MILK[1] LEVELS MGS.% A.M.	BULK MILK[1] LEVELS MGS.% P.M.
1	0.3				
2	0.3	10	10.6	2.4	2.6
3	0.2	14.4	10.6	4.2	3.4
4	0.2	10.4	8.6	2.8	2.6
5	0.2	10.2	9.4	3.4	3.0
6	0.2	10		3.2	
7	0.2		8.4	2.8	3.6
8	0.2		8.0	2.9	2.4
Average		11.0	8.9	3.1	2.9
9		9.0		2.5	1.8
10		3.2		1.2	

[1] Estimations were also made on foremilk samples from each quarter but the levels did not differ materially from the bulk milk-levels.

TABLE XIII

AVERAGE BLOOD AND MILK-LEVELS FOLLOWING THE INOCULATION OF 0.05 GM./KILO. OF SULPHAMEZATHINE SUSPENSION AND SODIUM SULPHAMEZATHINE SOLUTION INTO THE UDDERS OF THREE SHEEP.

DRUG	BLOOD-LEVELS MGS.% HOURS AFTER INJECTION 1/2	1	2	3	4	5	6	7	24	MILK-LEVELS 24 HRS MGS.%
Sulphamezathine Suspension	0.15	0.4	0.35	0.47	1.1	1.3	1.1		0.9	72
Sodium Sulphamezathine	1.37	2.07	3.3	3.87	4.27	3.0	2.33	1.67	0.27	12

at any one time contained the same percentage of sulphone, so only one figure is given (Table XII). The average morning level was 11 mgs. per cent., and the evening level 8.9 mgs. per cent., which, as one would expect from the results with single doses, is a greater difference than in calves, the morning and evening milk samples contained 3.1 and 2.9 mgs. per cent. of sulphone respectively. During this peroid the milk yield and appetite remained normal and there was no important change in the blood-picture (Table II). It appears from this evidence that even allowing for its three to four-fold greater potency, sulphone cannot be used in much smaller doses than sulphanilamide for the treatment of mastitis by oral dosing. It is well known, however, that when the udder is inflamed it loses, to some extent, its specific secretory powers and the "milk" resembles blood-serum more closely than normal milk. It was considered possible, therefore, that the milk-levels produced by sulphone in cows affected with mastitis might be higher than in normal cows. This belief was supported by the conclusion of McEwen *et al.* (1941) that sulphone was the more effective drug for the treatment of mastitis. Observations were therefore made on cows affected with mastitis and milk samples were taken by Mr. J. Berger, M.R.C.V.S., whilst he was treating them with sulphanilamide and sulphone. The cows received the standard initial dose of 90 gms. of sulphanilamide followed by one-third of this dose three times daily. Two of the six cows receiving sulphone were given doses of 90 gms. and the remainder 60 gms. once daily. The average milk-level in eighteen samples from thirteen animals receiving sulphanilamide was 4.6 mgs. per cent., and in seven samples from six animals receiving sulphone 2.5 mgs. per cent., which corresponds to a level of 8-10 mgs. per cent. of sulphanilamide. It will be seen, therefore, that even although the dose of sulphone was smaller than that of sulphanilamide, it produced milk-levels which were probably more effective.

Injection of Drugs into the Udder

It had been shown by McEwen (1940) that sulphonamide E.O.S. solution was more slowly absorbed from the udder than sulphanilamide suspension. This was perhaps a little surprising, and some preliminary studies were carried out in lactating ewes which were given doses of 0.05 gm./kilo. of drug (3-4 gms.) suspended or dissolved in 20 c.c. of distilled water; 10 c.c. were injected into each mammary gland. Three ewes were injected with sulphamezathine suspension and three with sodium sulphamezathine solution (although this is too irrittant for routine use), and blood samples taken at intervals. The sodium salt was rapidly absodbed and the blood-levels were similar to those following oral dosing, but the suspension was very poorly absorbed (Table XIII). It appears that although the sulphanilamide E.O.S. complex is poorly absorbed, the simple sodium salt of sulphamezathine is much more rapidly absorbed than a suspension. This is the result one would expect and the same findings were obtained in one cow.

Lactating Cows

Because of the high activity of sulphone against *Str. agalactiæ*, our chief work has been with this drug. Although we only have comparative data for sulphanilamide, the very low solubility of sulphone, together with its slow absorption from the gut, and slow excretion from the kidney, makes it appear unlikely that any

SULPHONE AND SULPHONE-BASE SUSPENSIONS INTO THE UDDERS OF LACTATING COWS.

Cow[2]	Drug	Dose gms.	Vol. c.c.	No. quarters	Hours in milk: 8	16	24	40	48	72
					mgs.%					
3-25	Sulphone	5	50	2		23.4	3.6	1.1		
4-11	"	5	"	1		15.0		2.4		
Average						20.6	3.6	1.5		
3-3	Sulphone	10	100	2		3.4	0.7	0.54	0	
3-7	"	10	"	2		13.6	3.6	1.3	0.16	0
4-4	"	"	"	2		75.0	7.0	1.8	3.8	Tr
4-7	"	"	"	2		21.0	4.8	1.6	1.1	0.16
6	"	"	"	1		61.2	10.6		1.4	0
12	"	"	"	2			14.0	2.0	10.0	Tr
Average						44.3	6.4	1.4	3.1	0.08
1-7	Sulphone E.O.S.	1	10	4		0.15	0			
2-8	"	2	"	1	0.6					
18-7	"	5	20	1		2.5				
1-12	"	5	50	2		22.6	0			
3-28	"	5	"	2		76	3.6	1.4	0	
Average						40 .	2.8	1.4	0	
6	Sulphone E.O.S.	9	90	1		7.0	14.0		0.86	0
2-8		10	50	1	2.1					
3-3	"	"	100	2		1.8	0.6	Tr	0	
3-7	"	"	"	2		19.6	2.0	1.6	2.2	Tr
3-17	"	"	"	2		44				
4-4	"	"	"	2		53.2	2.6	1.2	6.4	Tr
4-7	"	"	"	2		38.0	2.2	1.4	0.86	0
4-19	"	"	"	2		50.0	6.4	0		
12	"	"	"	2		23.4	2.0	1.2	2.9	Tr
IN	"	"	40	1		4.0	1.4		1.2	
15	"	12.5	25	2		73.5	15.5			
Average					2.1	34.3	5.3	0.91	2.2	0.2

[1] All suspensions were in water.
[2] Where two numbers are given the first refers to the cow and the second to the experiment number.

TABLE XV

BLOOD AND MILK-LEVELS (MGS.%) PRODUCED BY THE INJECTION OF 25 C.C. of a 40% SUSPENSION OF SULPHONE INTO ONE OR TWO QUARTERS OF LACTATING COWS.

Cow	No. quarters	Milk yield lbs daily	Blood levels: Days after injection 1	2	3	Milk levels: Days after injection 1	2	3
			mgs.%					
118	1	30	1.6	1.0	0.9	20.8	28.4	2.2
88	1	18	1.6	2.0	0.8	41.6	22.2	16.0
45	1	20	2.2	2.2	1.5	66.6	46.4	33.6
78	1	18	1.9	3.0	1.0	53.0	51.6	3.2
101	1	18	2.6	1.5	0.8	90.0	62	2.6
76	1	18	1.8	1.2		3.2	14.0	
74	2	18	2.8	2.2	1.5	46.8	25.0	18.8
92	2	15	1.9	1.6	1.9	28.4	27	17.4
Aver. (all cows)						40.9	32.07	11.7
Aver. (1 quarter)			1.95	1.8	1.0			
Aver. (2 quarters)			2.35	1.9	1.7			
* 92	1	20	1.6	1.2		13.0	9.6	

* In this experiment the drug was suspended in water, in all others in liquid paraffin.

TABLE XVI

MILK AND BLOOD LEVELS (MGS. %) PRODUCED FOLLOWING THE INJECTION OF VARIOUS PREPARATIONS OF SULPHONE AND SULPHANILAMIDE INTO THE UDDER[1] OF LACTATING COWS.

Medium	Dose per quarter	No. quarters injected	Drug		Blood-levels: Hours after injection 24	48	72	Milk-levels: Hours after injection 24	48	72
W	10	5	Sulphone	McEwen (1940)	1.76	0.72	0.19	10.39	4.42	1.3
W	10	11		This study				6.4	2.8	
W	10	2	Sulphone	McEwen (1940)	1.14	0.43		4.4	1.2	0.1
W	10	19		E.O.S. This study				5.3	2.2	
W	5	6	Sulphone	McEwen (1940)	0.65	0.1		2.62	0.2	
W	5	3		This study				3.6	1.0	
W	5	2	Sulphone	McEwen (1940)	0.65	0.06		2.65	0.05	
W	5	5		E.O.S. This study				2.8	0	
W	25	10	Sulpha-nilamide E.O.S.	McEwen (1940)	0.27			2.03	0.06	
W	12.5	3		" "	0.35			0.97	0	
LP[2]	10	10	Sulphone	This study	1.95	1.8	1.0	40.9	32.07	11.7

[1] In most instances, and in all where blood-levels are given, only one quarter was injected.
[2] In the previous studies fairly large samples of milk 200-1000 c.c. were removed at 10 or 16 hrs., and 30 or 40 hrs. as well as the intervals shown above. In this last series 5 c.c. samples were removed only at the intervals shown, until after 72 hrs. when 300 c.c. were removed.

TABLE XVII

AVERAGE MILK-LEVELS IN DRY COWS PRODUCED BY A SINGLE DOSE OF 20 GMS. OF SULPHONE SUSPENDED IN WATER OR LIQUID PARAFFIN.

Days after injection	12-15	16-20	26-31	32-52
Suspended in Water	1.2 (12)	1.15 (5)	3.5 (8)	0 (13)
Suspended in Liquid Paraffin		11.5 (8)		0.27 (9)

Figures in brackets indicate the number of quarters examined.

other drug would be more persistent in the udder. Even if it were, it would certainly not produce comparable blood-levels at the same time, a fact which may be important. Our own results are shown in Tables XIV and XV, and are summarised together with those of McEwen (1940) in Table XVI. In most of the work samples of 200-1,000 c.c. were taken at the usual milking intervals. Ten grammes of sulphone as a watery suspension produced much higher, and even five grammes higher milk and blood-levels than did 25 grammes of sulphanilamide (as the E.O.S. derivative), which has been shown by McEwen (1940) to be more slowly absorbed than sulphanilamide. The E.O.S. derivative of sulphone produced slightly lower blood- and milk-levels than did the suspension. It can be concluded that the E.O.S. derivative is more rapidly absorbed than the highly insoluble sulphone and the lower blood-levels confirm that following the injection of the E.O.S. complex it is absorbed as such, because we know that the complex is more rapidly excreted by the kidney than is the free sulphone. In the last series of experiments 10 gm. doses of sulphone suspended in liquid paraffin were injected into one (or in two instances, two) quarters of cows, giving 2-3 gallons of milk a day. These quarters were not milked and samples of only 5 c.c. were taken at 24 and 48 hours. After 72 hours samples of 300 c.c. were taken and the cows stripped out. The milk contained clots, but after two to four milkings it had become normal in quality and quantity. The milk-levels remained above 10 mgs. per cent. for three days (Table XV) which is much higher than in previous studies, a result no doubt partly due to the fact that the cows were not milked. The results with cow 92 (Table XV), however, in which a similar procedure was followed with sulphone suspended in water, indicates the absorption from liquid paraffin is slower than from water.

Dry Cows

The work in dry cows falls into two sections : that carried out in collaboration with Mr. J. Berger, in which one to four quarters of cows which had shown clots in their milk during the previous lactation were injected, and cows under our own immediate control, in which all four quarters were usually injected. The results obtained in collaboration with Berger are shown in Table XVII and our own results in Tables XVIII and XIX. No definite conclusions can be drawn concerning the rate of absorption from liquid paraffin and water respectively because of the irregular results, but there can be no doubt that the drug is very slowly absorbed from either medium and that liquid paraffin is the most suitable. Doses of 20 gms. per quarter produced effective milk-levels for three to four weeks and effective blood-levels for 9-12 days. With doses of 10 gms. effective milk-levels were maintained for about 14 days and blood-levels for about seven days. On two occasions 20 gms. of sulphone were injected into each quarter of a cow as the E.O.S. derivative. The blood-levels are shown in Table XX and it will be seen that absorption was very much more rapid than with the suspension, the blood-level falling below 1 mg. per cent. within two days.

Discussion and Summary

Blood-levels produced by repeated doses of sulphanilamide, sulphapyridine, sulphathiazole, sulphadiazine, sulphamerazine, sulphamezathine and 4 : 4′ diamino diphenyl sulphone in the calf have been determined (Tables I and IV). Blood-levels produced by repeated doses of selected sulphonamides in the sheep, pig and

TABLE XX

BLOOD-LEVELS IN DRY COWS PRODUCED BY THE INJECTION OF 20 GMS. OF SULPHONE AS THE E.O.S. DERIVATIVE INTO EACH QUARTER.

	HOURS								
	1	2	3	5	7	24	48	72	120
COW A	16	19.2	15.6	9.0	-	3.6	1.0	0.46	Nil
COW B	19.2	18.8	14.4	10.2	5.6	4.8	0.6		
Aver.	17.6	19.0	14.0	9.6	5.6	4.2	0.8	0.46	Nil

TABLE XVIII

AVERAGE MILK-LEVELS IN DRY COWS INJECTED WITH SULPHONE SUSPENDED IN 50-100 C.C. OF WATER OR LIQUID PARAFFIN.

DOSE GMS.	MEDIUM	TIME IN DAYS							
		1	2	3	4	5	6	8	12	14
		MGS. %								
10	W		24.72 (4)		5.2 (2)		11.6 (2)	0.6 (4)		
10	L.P	19.2 (5)	34.0 (4)	47.4 (4)		25.8 (5)		23.9 (5)	2.8 (5)	
20	W							8,000 (2)	86.9 (4)	3.6 (2)
20	L.P	1.0 (7)							21.0 (7)	

The numbers in brackets indicate the number of quarters examined.

TABLE XIX

BLOOD AND MILK-LEVELS PRODUCED BY THE INJECTION OF SUSPENSIONS OF SULPHONE SUSPENDED IN WATER OR LIQUID PARAFFIN INTO ALL FOUR QUARTERS OF DRY COWS.

COW	MEDIUM	DOSE	DAYS												
			1	3	5	7	9	10	12	15	21	22	14	22
			BLOOD-LEVELS MGS.%										MILK. MGS.%	
12	LP	12.5 cc.	2.8	2.4	1.9	0.5	Nil		Nil				0.6	
19	"	5 gms.	3.6	1.8	1.6	0.4	"		0.4				4.0	
24	"		4.6	4.0	2.4	0.3	"		0.6				5.2	
Average			3.66	2.73	1.97	0.33	Nil		0.33				3.3	
98	LP	25 cc.	2.4	2.0	1.7	1.5	Nil		Nil				27.4	
26	"	10 gms.	3.2	3.4	2.4	0.2	"		"				2.8	
28	"		3.6	4.2	5.3	1.6	"		1.0				1.8	
Average			3.06	3.2	2.47	1.1	Nil		0.33				10.7	
114	LP	30 cc.	4.4	2.0	1.6	1.6	1.5	0.8	0.8	1.2				5.8
102	W	20 gms.	3.6	5.6	4.0	2.2	3.2	1.8	3.6	0.8		0.8		40.8
113	W		3.0	3.0	2.4	1.8	1.6	1.6	1.8	2.8		2.0		1,200
2	W		1.4	4.0	4.8	2.0	2.6	0.7	0.4					
28	W		1.6	2.0	1.6		4.0			3.0	0.6			
Average			2.8	3.32	2.96	2.35	2.38	1.2	1.6	1.9	0.6	0.5		444.9

horse, and blood- and milk-levels in the cow, have been determined. The results confirm that sulphone, sulphamerazine and sulphamezathine produced better blood-levels than the other sulphonamides in domestic animals.

The common enteric, septicæmic and pneumonic diseases of animals are caused by Gram-negative organisms. The relative value of the sulphonamides in these conditions has been discussed in detail by Francis (1947) on the basis of evidence presented in this paper and elsewhere. Sulphamerazine, sulphamezathine and sulphadiazine will probably be the most effective drugs. Apart from the relatively low potency of sulphone against Gram-negative organisms, it is more toxic for other species than it is for cattle.

The present study indicates that multiple daily doses of the sulphonamides are not necessary in the farm animals. An initial dose of 0.1-0.2 gm./kilo.* of sulphamezathine or sulphamerazine followed by a daily dose of 0.05-0.1 gm./kilo. is adequate. In the calf these doses certainly need not be given more than once daily and probably not in the pig when sulphamezathine is used. Sulphamezathine is the most persistent of all the sulphonamides in the pig and the sodium salt can conveniently be given subcutaneously or intraperitoneally and need only be given once daily. To produce equal blood-levels the other sulphonamides would have to be given in more frequent doses. In the horse and the sheep doses should be given twice daily and the total daily dose should not be less than 0.1 gm./kilo. Both pigs and horses appear to eat sulphamezathine, sulphamerazine, sulphadiazine and sulphone more readily than the other sulphonamides.

Sulphone is very well tolerated by the bovine and it has been shown by Francis, Peters and Davies (1947) that it is the most potent of the sulphonamides against *Str. agalactiæ*. Unfortunately, the milk-levels produced by oral dosing are lower than the blood-levels, but the drug may still have a place in the treatment of mastitis by this route because of its low toxicity.

It was confirmed (in a single experiment not reported in this paper) that the E.O.S. derivative of sulphanilamide was more slowly absorbed from the udder than sulphanilamide. On the other hand, the sodium salts of the sulphonamides were more rapidly absorbed than the suspensions and in any event were too irritant for routine use. The E.O.S. derivative of sulphone was, however, absorbed at about the same rate as the suspension from the lactating udder, but was much more rapidly absorbed than the suspension from the dry udder. Sulphone was about ten times more persistent in the cow's udder than sulphanilamide and probably the most persistent of all the sulphonamides. A dose of 10 gms. infused into a lactating quarter, or one affected with mastitis, may be left for 2-3 days and during this period maintains high milk concentrations and relatively high blood concentrations. Doses of 10-20 gms. infused into all quarters of dry cows produced effective milk concentrations for long periods and blood concentrations for 7-12 days. These facts combined with its high antibacterial potency leave little doubt that it will be the sulphonamide of choice for infusion into the cow's udder.

I am indebted to W. Russell and F. Vernon for their assistance with this work.

* A dose of 0.1 gm./kilo. corresponds to a dose of 1 drachm per 60 lb. or 1 ounce per 6 cwt.

REFERENCES

Berger, J. (1945): Personal communication.

Francis, J. (1947): "Bacterial Chemotherapy in Veterinary Medicine." *Vet. Rec., 59,* 131-137. Some observations on the blood- and milk-levels produced by 4 : 4′ diaminodiphenyl sulphone, 4 : 4′ nitroamino diphenyl sulphone and the common sulphonamides in various domestic animals. In press.

Francis, J., Peters, J., and Davies, O. L. (1947): *J. Comp. Path.* In press.

McEwen, A. D. (1940): Personal communication.

McEwen, A. D., Pizer, N. H., and Paterson, J. D. (1941): "Preliminary Trials on the Administration of Sulphanilamide E.O.S. and 4 : 4′ diamino-diphenyl sulphone to Normal Cattle and to Cattle affected with Streptococcal Mastitis." *Vet. Rec., 53,* 429-436.

Rose, F. L. (1945): Personal communication.

THE TREATMENT OF HEPATIC COCCIDIOSIS IN RABBITS

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Serious losses from hepatic coccidiosis occur among rabbits in commercial rabbitries, but until recently little work appears to have been done on the treatment of the disease. The recent advances in the chemotherapy of protozoan diseases have not passed completely unnoticed by workers on rabbit coccidiosis, however, and satisfactory therapeutical control by the use of atebrin was reported by Gallo and Loreto in 1940. It has not been possible to consult the original paper and the following summary of their results was obtained from an abstract which, unfortunately, gave no information as to the numbers of rabbits employed in the experiments. One trial concerned 12 to 15-day-old rabbits, born of infected parents that had been kept in uncleaned cages until the young were born. Half of these young rabbits received three intravenous injections of 0.5 ml. of atebrin in a 1 : 1,000 solution, as a result of which treatment they remained healthy, although 90 per cent. of the other half, which were untreated, died of coccidiosis. Equally successful results were subsequently obtained in artificially-infected rabbits aged from one to two months for which the dose rate had been increased to 1.0 ml. of the 1 : 1,000 solution. Other reports of successful treatment include those of Marotel and Guilhon (1941), who claimed that quinacrine and thymol gave good clinical results, and those of Seek and Schumacher (1941), who reported success from a drug named " Eimeran," but we have been unable to trace any account of the chemistry of the substance. Koffman (1943) tested the efficacy of phenothiazine and found that treatment did not interfere with the subsequent development of oocysts in the fæces and that mortality was greater among the controls.

Sulphonamides, which have proved so successful in chicken coccidiosis, were not tried until 1943 when Joshua reported that sulphaguanidine was satisfactory in a dose of 0.5 g. per kilogram body-weight once daily in the mash on two successive days and that rabbits are able to tolerate one gram per kilogram by this method. This two-day treatment may be repeated three times without danger, although sulphaguanidine is toxic to rabbits as was shown by Corwin (1941). This worker found that sulphaguanidine is readily absorbed and excessively acetylated, and that the very high concentrations of the drug in the blood caused death in 80 per cent. of the animals within eight days, autopsy revealing renal, splenic,

and hepatic lesions. Jankiewicz (1945a) reported that hepatic coccidiosis could be prevented by daily dosing of sulphasuxadine (succinyl sulphathiazole), but that this drug was moderately toxic when given over a period of thirty-two consecutive days. Following on the good results obtained by Horton-Smith and Taylor (1942, 1943, 1945) and Horton-Smith and Boyland (1946, 1946a) with sulphamezathine and sulphapyrazine in controlling cæcal coccidiosis in chickens, it was decided to test the efficacy of these drugs on the hepatic form of coccidiosis in rabbits due to heavy infestations of *Eimeria stiedæ*.

General Methods

Oocysts of *Eimeria stiedæ* were obtained from naturally heavily-infected rabbits, the livers and gall-bladders of which were removed and passed through a meat mincer. The minced liver-tissue was then soaked in water, shaken up with glass beads, and squeezed through three layers of muslin, the filtrate spun in the centrifuge, and the oocysts collected by flotation in salt solution, and washed several times in water. Sporulation was then allowed to take place in a 2.5 per cent. solution of potassium bichromate in petri plates. After five days at room temperature the number of sporulated oocysts was counted and the predetermined dose administered by stomach tube. The assessment of the degree of infection at post-mortem examination was carried out by observing the number of lesions present, the numbers of oocysts in the gall-bladders and in the filtrate derived from the minced liver-tissue, and the relative weight of the liver. Treated groups received the medicated ration as their first meal of the day.

Experimental

The experiments were undertaken to test the effects of sulphamezathine on infections of *E. stiedæ* in rabbits which were offered a ration containing the drug (1) before they were heavily infected, (2) immediately after being heavily infected, and (3) at various intervals after receiving heavy infections to determine the time treatment might be delayed and yet prove effective. Sulphapyrazine was added to the food of one group in Experiment 5.

Experiment 1.—Rabbits having access to sulphamezathine before receiving heavy infections with sporulated oocysts of E. stiedæ.

To ascertain whether sulphamezathine would prevent rabbits from becoming seriously infected, one group of seven six to eight-weeks-old rabbits was offered a ration containing 1.0 per cent. sulphamezathine for three days, after which this and a control group of seven rabbits on ordinary diet received two million sporulated oocysts of *E. stiedæ*. Sulphamezathine was fed for the duration of the experiment. On the 23rd, 24th, 25th and 26th days after inoculation with oocysts three deaths from severe hepatic coccidiosis occurred in the control group. The rabbits in both the control and treated groups were killed and examined five weeks after inoculation. Post-mortem examination gave no indication of infection in any of the rabbits which had been under treatment and the proportion of *liver: body-weight* averaged 5 per cent.; the normal proportion in healthy rabbits

lies between 5 and 6 per cent. In the control group, on the other hand, two rabbits were found to be severely affected and to show a proportion of *liver: body-weight* of 15 per cent. Lesions were also present in the two less severely affected rabbits in which the *liver: body-weight* was found to be 7 per cent.

The results of this experiment show that sulphamezathine is an efficient preventive against infections with *E. stiedæ*.

Experiment 2.—Rabbits having access to sulphamezathine one day after receiving heavy infections with sporulated oocysts of E. stiedæ.

To determine whether sulphamezathine was active against early existing infections, two groups of seventeen six to eight-week-old rabbits were infected with two million sporulated oocysts of *E. stiedæ*. The day after they were infected one group was offered a mash containing 1.0 per cent. sulphamezathine once each day. This group was maintained on the medicated ration until the end of the experiment twenty days later. Deaths began in the control group as early as the ninth day after inoculation and continued on the 12th, 16th, 18th, 21st and 22nd days. No deaths occurred in the treated group. The survivors of both groups were killed and examined on the 27th day after inoculation. The post-mortem findings are summarised in Table I.

TABLE I

The results of post-mortem examinations of rabbits artificially infected with *E. stiedæ*, half of the number being treated with sulphamezathine, the other half being kept as controls.

Controls			Treated		
Number of rabbit	Post-mortem findings	*Liver-weight to body-weight* expressed as percentages	Number of rabbit	Post-mortem findings	*Liver-weight to body-weight* expressed as percentages
1	+ (D)	10.0	18	—	4.3
2	+ (D)	11.0	19	—	3.6
3	+ (D)	10.0	20	—	4.0
4	+ (D)	8.3	21	—	6.3
5	+ (D)	10.0	22	—	3.8
6	+ (D)	14.2	23	—	6.3
7	+ (D)	20.0	24	—	4.3
8	+ (D)	18.0	25	—	4.2
9	+ (D)	20.0	26	—	4.2
10	+ (D)	18.1	27	—	5.5
11	+	9.0	28	—	4.2
12	+	11.0	29	—	4.0
13	—	5.0	30	—	4.0
14	—	6.3	31	—	6.0
15	—	5.0	32	—	5.5
16	—	5.3	33	—	6.25
17	—	5.0	34	—	6.25

(D) = died.
+ = presence of coccidiosis.

The results of this experiment show that sulphamezathine is effective in controlling early infections of *E. stiedæ* and that it might prove equally effective in treating well-established ones.

Experiment 3.—Rabbits having access to sulphamezathine from the fifth or tenth day after receiving heavy infections with sporulated oocysts of E. stiedæ.

In an attempt to determine the extent to which sulphamezathine is capable of controlling well-established infections with *E. stiedæ* twenty rabbits of six to eight weeks of age were divided into four groups of five. The rabbits in three of these groups were infected with 100,000 oocysts and one of the groups was offered 1.0 per cent. sulphamezathine in the food from the fifth day and the other was not offered the medicated ration until the tenth day after inoculation. The third group received no sulphamezathine and served as a control group. The fourth group was not infected and was reserved as a control group to the second part of the experiment. Three rabbits of the control (third) group succumbed and there were gross lesions in the livers whose relative weights averaged 11.6 per cent. of the total body-weight. The other two surviving rabbits of the control group were killed and only minor infections were evident. No deaths occurred in the two treated groups.

Fifteen days after the last death from coccidiosis all the rabbits from groups one and two and the hitherto uninfected rabbits of group four were infected with one million oocysts. None of the rabbits in groups one and two died as a result of this infection and the livers were normal in size and showed only a few scattered lesions. The control rabbits of group four, however, became heavily infected and four of the five died from severe hepatic coccidiosis on the 20th, 22nd and 23rd day after inoculation; the single survivor of this group proved to be only lightly infected.

These results appear to indicate that treatment with sulphamezathine is effective in controlling well-established infections with *E. stiedæ* and that rabbits surviving hepatic coccidiosis as a result of the treatment were immune to further serious infections with the same species.

Experiment 4.—Rabbits having access to sulphamezathine from the fifteenth day after receiving heavy infections with sporulated oocysts of E. stiedæ.

Two groups of five six to eight-week-old rabbits each were given 100,000 sporulated oocysts and one of these groups received 1.0 per cent. sulphamezathine in the food at the end of the fifteenth day of infection. At autopsy, which was carried out one month after infection, four of the rabbits from each group showed equally gross lesions and the other three, one from each group, showed equally light infections.

These results indicate that treatment of a very advanced infection is valueless.

Experiment 5.—Rabbits having access to sulphamezathine and sulphapyrazine from the tenth day after receiving heavy infections with sporulated oocysts of E. stiedæ.

Twenty-four six to eight-week-old rabbits were each infected with a million sporulated oocysts. Ten days later these were divided into groups of six and

treated as follows: (a) given access to 0.5 per cent. sulphamezathine in the food for the remainder of the experiment; (b) given access to 0.25 per cent. sulphamezathine in the food for the remainder of the experiment; (c) given access to 0.25 per cent. suluphapyrazine in the food for the remainder of the experiment; (d) a control group which received no medicated food. Another group of six rabbits was not infected and was maintained on normal food. The rabbits from all groups were killed and examined one month after the initial infection, the results of the examinations being given in Table II.

TABLE II

The results of *post-mortem* examinations of artificially infected rabbits which had been treated with sulphamezathine or sulphapyrazine from the tenth day of infection and of untreated infected and uninfected control rabbits.

Particulars of Treatment							Untreated Controls					
0.25 per cent. sulphamezathine			0.5 per cent. sulphamezathine		0.25 per cent. sulphapyrazine		Infected			Uninfected		
Number of rabbit	Degree of infection	Liver-weight as percentage of body-weight	Degree of infection	Liver-weight as percentage of body-weight	Degree of infection	Liver-weight as percentage of body-weight	Number of rabbit	Degree of infection	Liver-weight as percentage of body-weight	Degree of infection	Liver-weight as percentage of body-weight
1	+	7.0	—	4.0	—	4.2	1	++++(D)	15.0	—	6.5
2	—	6.0	++	7.0	+	7.0	2	++++	11.5	—	6.5
3	+++	7.5	—	3.8	—	3.2	3	++++	10.5	—	6.0
4	—	5.0	—	3.3	+++	8.0	4	—	6.0	—	6.0
5	++	7.0	—	3.6	—	3.0	5	++++	10.5	—	5.0
6	++	6.5	—	4.7	—	3.0	6	+++	9.0	—	6.0
Average percentage of *liver-weight to body-weight*		6.5		4.4		4.7			10.4		6.0

\+ = few visible lesions but many oocysts present.
++ = half of liver affected.
+++ = three-quarters of liver affected.
++++ = whole of liver affected.
(D) = died.

These results indicate that 0.5 per cent. sulphamezathine and 0.25 per cent. sulphapyrazine are of value in checking advanced infections with *E. stiedæ*.

Discussion

The results obtained in Experiment 1 indicate very clearly that sulphamezathine is effective in preventing what might otherwise prove to be fatal infections with *E. stiedæ*. That sulphamezathine is active against early infections is shown in the results of Experiment 2. Experiment 3 shows that treatment is effective even when postponed until the tenth day after inoculation and, although the point needs confirmation, there is some evidence that treated survivors of heavy infections are immune to later infections with the same species, such as would prove

fatal to susceptible rabbits. This is in agreement with the findings of Horton-Smith and Taylor (1945) and Horton-Smith and Boyland (1946 and 1946a), which showed that chickens surviving heavy infections with *E. tenella* as a result of treatment with sulphamezathine and sulphapyrazine are, for a time, resistant to fatal infections with the same species. The results of Experiment 4 indicate that if treatment is postponed to the fifteenth day after inoculation no apparent benefit ensues. The findings in Experiment 5 suggest that pathogenic infestations of a lighter order are controlled by sulphamezathine and sulphapyrazine when added in the proportions of 0.5 and 0.25 per cent. respectively to the food even when treatment is postponed until the tenth day after infection.

In assessing the degree of infection in the above cases it is pertinent to recall the observations of Jankiewicz (1945) who found that the liver of a rabbit which had received 100,000 oocysts of *E. stiedæ* constituted 20.5 per cent. of the body-weight, there being a corresponding increase in the number of gross lesions in the bile ducts and a decrease of normal liver-tissue visible on the surface. Using these criteria to assess the extent of liver damage, it appears that 0.25 per cent. sulphamezathine is also of benefit and would probably be effective in controlling infections of relatively smaller magnitude more commonly met with in the field.

In view of the effectiveness of treatment, even after a delay of ten days from the time of infection, it appears to be necessary for a certain blood concentration of the drug to be reached before coccidiostatic action takes place and that this level must be attained before the development of the later stages of schizogony. It may be that merozoite-formation in the late schizont is at least temporarily suppressed as was observed by Horton-Smith and Taylor (1945) in the schizogonous stages of *E. tenella* in the cæca of chickens. We have as yet no knowledge of any undesirable side-effects which the drugs may produce when administered over long periods, but so far there is no evidence that sulphamezathine produces the conditions in rabbits described by Corwin (1941) in the use of sulphaguanidine, and it is concluded that sulphamezathine and probably sulphapyrazine are of practical value in controlling epidemics of hepatic coccidiosis. The cost of such treatment would amount to approximately twopence or threepence per day for a rabbit weighing two kilograms.

Summary

1. Sulphamezathine incorporated in the food in the proportion of 1.0 per cent. is effective in preventing disease after infection with the oocysts of *E. stiedæ* in numbers that would otherwise prove fatal.

2. This preventive treatment is effective in controlling severe hepatic coccidiosis even if postponed up to ten days after inoculation with sporulated oocysts, but not if postponed for 15 days. In less massive infections 0.5 per cent. sulphamezathine or 0.25 per cent. sulphapyrazine administered in the same way are also effective in controlling the disease and after a similar delay.

3. Some evidence was also obtained to show that rabbits which have survived a heavy infection of *E. stiedæ* as a result of treatment with effective sulphonamides are subsequently resistant to fatal infections with the same species.

REFERENCES
Corwin, W. C. (1941): *Bull. Johns Hopkins Hospital*, 69, 39.
Gallo, P., and Loreto, F. de A. (1940): *Rev. Med. Vet. Parasit.*, Caracas, *2*, 99. (From abstract in the *Veterinary Bulletin*, *12*, 512.)
Horton-Smith, C., and Taylor, E. L. (1942): *Vet. Rec.*, *54*, 516.
Horton-Smith, C., and Taylor, E. L. (1943): *Vet. Rec.*, *55*, 109.
Horton-Smith, C., and Taylor, E. L. (1945): *Vet. Rec.*, *57*, 35.
Horton-Smith, C., and Boyland, E. (1946): *Brit. J. Pharmacol.*, *1*, 139.
Horton-Smith, C., and Boyland, E. (1946a): *Poult. Sci.*, *25*, 390.
Jankiewicz, H. A. (1945): *J. Parasit.* (supplement), *31*, 8.
Jankiewicz, H. A. (1945a): *J. Parasit.* (supplement), *31*, 15.
Joshua, Joan O. (1943): *Vet. Rec.*, *55*, 149.
Koffman, M. (1943): *Skand. Vet. Tidskr.*, *33*, 69.
Marotel, G., and Guilhon, J. (1941): *Rec. Med. Vet. exot.*, *117*, 320.
Seek, P., and Schumacher, W. (1941): *Arch. Kleintierzucht.*, *2*, 57.

REMARKS ON SOME NON-ACUTE CONDITIONS GIVING RISE TO LAMENESS IN THE HORSE*

By J. McCUNN, M.R.C.V.S., L.R.C.P.
Royal Veterinary College

WHEN one visits Lincoln I think that the talk should be either about Lincoln Reds, the Cathedral or horses. Of Lincoln Reds one can only talk in praise, for it is common knowledge that they are so wonderful that they rarely have anything wrong and time is too short to set a bunch of enthusiasts agog. As regards the Cathedral, I expect that you should know all about it, but strange to relate, when I was having my hair cut in the lower town some two years ago I ventured to ask the old barber a few questions about the venerable edifice, and in particular about Sir William Robertson, that great Lincolnshire man who is commemorated therein. To my utter astonishment the old man, although he had lived in Lincoln for many years, had never been up the hill and he had never heard of Sir William. So just in case I should get another shock we will leave the Cathedral alone in its majesty.

So I feel constrained to talk about horses and that is good, for I like to talk horses. Is was brought up not very far from here in a community where, except at election times, everybody talked horses, and even the gardeners and the men at the gasworks considered themselves to be authorities. I doubt if I would have joined the profession if it had meant that I was to be a cow leach. Nowadays I feel that it is a duty to try and focus attention on the horse every now and then, for the moderns are apt to forget his existence.

I have chosen lameness for my theme, particularly some cases of obscure origin and in the fore limb. The diagnosis and location of the seat of lameness is a job in which we can employ all our faculties of sight, touch and hearing and apply our anatomical, physiological and pathological knowledge. It is a job in which we have to appreciate facts and assess the value of circumstantial evidence in order to build up a case and come to a conclusion. Indeed, the ability to diagnose the seat of trouble, or at any rate to give a reasonable explanation, may make or mar a practitioner in the eyes of his clients. There is an unfortunate feature in obscure lame cases. In those in which one's efforts to promote recovery prove successful one is never certain that the diagnosis was correct. I have purposely chosen non-acute lameness for these are the cases which give me most trouble and anxiety.

* Address delivered to the Lincolnshire Veterinary Medical Association.

I will put to you a series of unusual lamenesses, and I will group them into four classes of types. All my cases have been observed in young horses.

First, there is the horse which will go all correct, a good 1234 when in hand, yet put him in harness and after going a short distance he will be lame, generally in one but sometimes in both fore limbs. Take him out of harness, rest for a while, and then try him in hand again. Do what you will he will go sound. His legs will be clean and equal and a manual examination will give no lead to the site or cause of the trouble. Put him in harness again and the lameness reappears. I have noticed that such horses when in harness exhibit a tendency to bore to the lame side, to drop the shoulder a little, take a shorter step with and catch the toe of the affected limb. I have noticed also that they show a sharper than usual skin reflex over the scapular area. Going on the assumption that the trouble may be due to collar pressure on the supra scapular nerve as it turns around the anterior border of the scapular, I have replaced the ordinary neck collar with a breast one, and with satisfactory results. Later on I have found that when these animals have conditioned and muscled up it is possible to revert to a neck collar.

Secondly, there is the case which is exactly the opposite of my first illustration. The horse will be lame in hand or in the field. If stalled he may point his foot. Put him in harness and at work and the lameness will go. If kept at regular work he will work the lameness off, not only temporarily but permanently. As in the first illustration, I have been at a loss to find any obvious malformation or defect in the limb. For an explanation I have toyed with the idea that the trouble may be synovial in origin, i.e., adhesions in the fringes, which under forced weight, drawing exercise, are separated or broken down in the same way as are those of man under the dramatic manipulations of the osteopath.

Thirdly, I will draw your attention to a shoulder lameness which occurs in young riding horses which are subjected to the strenuous schooling which is required in order to fit them for police or similar work. You will occasionally see it also in the young stallion which is given too much lunging exercise. In my experience this lameness occurs in the near fore. In time the spinatus muscles will waste although the supra scapular nerve may appear to be all right. I believe that this lameness is seated in the epiphyseal junctions which, owing to the continued abnormal and unbalanced muscular stress or effort in the school or lunging circle, become slightly separated. If the shoulder be forcibly extended, you will get definite evidence of flinching. In passing I might mention that I have seen two cases of a similar nature in young bulls.

Fourthly, there is the case where the horse will be lame first in one leg and then in another one; what is often called metastatic lameness. He will not be acutely lame, but it is quite sufficient to prevent him working. Young horses are affected. I have seen a number of such cases and I think that you can classify them into two groups.

A. Those which show slight enlargement in the epiphyseal regions, especially at the lower end of the radius, and apple joints at the fetlocks.

B. Those which show a slight diffuse thickening and tenderness of the tendon sheaths with apparently no increase in the size of the tendon underneath. If the foot be picked up and the tendons manipulated, faint superficial crepetations can

be felt or, better still, heard under the stethoscope. These are the typical signs of a teno synovitis.

In both cases the step is shortened and they are lame coming off the ground. In the second group there is a noticeable diminution of flexion at the fetlock when at the trot. In the first group I have seen good results follow the addition of cod liver oil to the diet or when turned out on fresh spring grass. This points to some dietary factor. In the second group you will often find that the animals are positive to B. Abortus or Streptococcus viridens and a course of the appropriate vaccine will lead to resolution. It is well to attend to the diet on these cases also.

I think that dietary defects are a very potent factor in lameness in town horses, especially in the young-toothed. It is remarkable how, if the age is all right, strained tendons and big joints fine down if the patient is turned out on young spring or early summer grass. I would advise all town horse owners to have a definite roster for turning out, and not to wait until it has to be done for reason of injury. I am confident that every month's turn out, especially if in the spring, adds another potential year to the total period of service. In studs where this is done it pays good dividends.

The good effects are particularly reflected in the bone and tendons below the knee and the hock and in the feet. The horn of the hoof is rejuvenated in texture and elasticity to that of a three-year-old. These points are of particular importance when one remembers that a considerable proportion of the town horse casualties arise from the dysfunction and abnormalities of these parts.

The Elbow Joint

I have seen two cases of lameness in which the seat of trouble was in the interior of the elbow joint. In both cases there were no macroscopic changes in the limbs discovered during life. The first case was in a six-year-old and it was unsolved until the *post-mortem*. The horse had been involved in an accident whilst being unloaded at a railway dock. His fore feet slipped between the box and the dock. He was released with difficulty. There was little apparent injury apart from a few superficial bruises and scratches and he went sound. Some time later he began to go lame in the near fore, a groggy type of lameness. He exhibited a symptom which I could not explain. Whilst in the stall he would crouch slightly on the affected limb every now and then. I could do no good with him and he was destroyed. The P.M. revealed an ulcerated state of the articular cartilage of both humerus and radius.

Some time later I was browsing in that wonderful book on "Lameness in the Horse" by William Percival (1849). In this he describes a case of elbow-joint lameness occurring in one of his own horses. One of the symptoms he noted he described as "a remarkable crouching sort of action dreading almost to move his limbs forward." Bearing this and my own experience in mind, I was on the look-out for case No. 2. It turned up. The horse was groggy both fore; he would loosen up with exercise, but after a rest was groggy again, especially so at the move off. Now this horse exhibited the crouching action whilst in the stable. Every now and then he would crouch and flex the knees as if he was about to lie down. When not doing this he kept his knees slightly flexed. In the absence of any obvious defect in the limbs, I made a diagnosis of ulceration in the elbow

joint. The horse was an old one and was destroyed. At the P.M. I found extensive ulceration of the articular cartilage of both humerus and radius. These are the only cases I have seen and had under observation in life, but in the slaughterhouse, etc., I have frequently seen ulcerations and erosions of articular areas in this and other joints, particularly the tibio astragaloid joint, in old horses, which, to the best of my information, did not show any signs of lameness prior to slaughter.

Supra Carpal Check Ligament

Leaving the elbow and passing down the limb we come to another site which is occasionally a seat of trouble. I refer to the supra carpal check ligament, i.e., the supra carpal band of the superficial flexor. We are wont to pay full attention to the infra-carpal check ligament and almost ignore the superior one. The latter ligament can be the subject of strain, particularly at its muscular end. The lameness produced is not very marked; it is exhibited by a diminished flexion of the carpus when the action of that joint is compared with its fellow of the opposite limb. It is to be noted best from the lateral view. Slight pain is shown if the part is pinched between the thumb and finger, and this reaction is often the first sign to draw attention to the part. I have met the trouble in light and riding horses; never in heavy draught. Time seems to be the best healer for I have had little success with local applications.

The Pisiform

The Pisiform bone is sometimes injured. The injury may be direct, and occasionally the bone may be fractured. This form gives little trouble to the diagnostician for lameness is marked and there is considerable local heat, swelling and pain. The injury may be indirect following sudden muscular violence with separation of the external or medium flexor tendons at the point of insertion. The horse is disinclined to extend the knee and this is best shown after a sharp gallop; there may be little lameness at a cold trot or walk. The step is lengthened and circumduction will be noted. At rest in the stable the limb will be kept level with or a little in retard of its fellow and rested on the toe. These cases are not promising, being almost as difficult to resolve as is carpitis. I have found a long turn out to be best; rest in the stable only leads to an increase in the stiffness.

Synovitis of the Fetlock Joint

Some years ago when the " Page field system " of dust collection was introduced into a certain borough, there were many cases of lameness. The fetlock joints were affected. There was considerable swelling and a great increase in the synovial content of the pouches between sesamoids and metacarpus. Horses would come in sound, and be found lame the next morning. If the leg was picked up and the fetlock flexed, the sesamoids appeared to be " floating in fluid " just as the patella does in certain synorial lesions in the human knee. If they were struck they would float forwards and tap the metarcarpus. The foot was rested on the toe. There was obvious diminution on flexion at the fetlock and the step lengthened with some circumduction of the limb.

The condition was liable to become chronic. On P.M. on one or two which were slaughtered, for they were aged, the synovia was in excessive amount, in colour bright yellow with touches of green, and the articular surfaces were stained

similarly. Resolution was protracted but fortunately we came upon the cause and so ended the trouble. The dustmen objected to the new system and to sabotage it had worked the vehicles with the brakes screwed up.

Pedal Ostitis and Navicular Disease

These lesions are often associated.

Pedal ostitis may occur on its own, but I think that with navicular disease there is always some pedal ostitis. Pedal ostitis is a very common cause of lameness in riding horses. The bone has the appearance of having been the seat of an inflammatory reaction. The Ventral aspect of the Ospedis, especially the wings, show many small osteophytes. In life the horse goes tender. There may be a little heat and when at rest the horse will point first one foot and then the other. Even when not pointing he will rock the foot uneasily. The type of foot affected is that with the low heel with the hair line near the ground, and a poor dome to the sole. As a rule there is no contraction at the heel.

This is also the foot which is subject to navicular disease. The blocky, so-called navicular foot is seen in the later stages and is produced as a result of nature's efforts to alleviate pressure on the navicular area. The heel deepens, the frog atrophies and rises, the heels contract and the frog loses contact with level ground. In pedal ostitis we find the shoe wears at the heel and toe; in early navicular it wears at the toe. In later navicular cases, as flexion below the fetlock diminishes, the foot is put down like a block and so the shoe wears level all over; sometimes they will wear to as thin as a sixpence.

Feet affected with pedal ostitis foot are more sensitive to the hammer or pinchers, and they are more inclined to be odd than are navicular feet. A navicular foot tends to develop a waist about a third of the way down. This waist is often patent to the naked eye and always so to the fingers.

Horses lame from pedal ostitis often develop small deep-seated corns.

Horses lame in the foot often show changes in the fetlock joint, i.e., some synovitis. This may be more obvious than the original foot trouble. I have noted that this secondary fetlock trouble may be associated with lesions in sites other than the feet as, for instance, pelvic injuries. This secondary feature is occasioned by the unusual or abnormal stress placed upon the joint consequent upon interference with the normal functions of the more distal articulations.

Another type of chronic lameness is seen in the horse with a tender or thin sole. He will go very feeling especially on loose gravel. Nine times out of ten he has a poor heel and small deep-seated corns. A considerable number of the cross-bred type have such feet. The only way to keep them sound is to give plenty of cover in the shoe. Normal hunting shoes are practically useless. They should never be turned out unshod in front. I have seen them walking in the hard, dry fields in July and August like cats, and seen a picture like a sunset when the soles have been pared out. Whilst dealing with this I would draw attention to the corn. I do not mean the corn which is obvious, but rather the small deep-seated affair which one has to dig to find. They are well back in the bar-wall angle, sometimes under the bar. The discoloration does not seem to extend to the superficial layers of horn. Within the last few weeks I have seen two such cases, both diagnosed previously as navicular disease.

In our attempt to come to a conclusion as to the site or nature of a lesion in the foot, we can gain useful information from an inspection of the shoe. The average horse with a normal foot will wear the outside toe area. The early navicular case wears at the toe, the late case more or less evenly all over. In Keratoma and Pyramedal disease wear is at the heel. Early ring bone at the toe and heel, later mostly at the heel. In corn the outside branch is worn. No doubt these abnormalities in wear occur as a result of the horse trying to ease the affected part. In surgical shoeing we should bear these observations in mind and profit thereby.

In chronic foot cases an inspection of the fore-arms will show that they are unequal. There will be muscular wasting in the fore-arm of the lame limb. It may be evident to the naked eye; if not the tape measure will demonstrate it. Many animals will flinch obviously to the hammer; others not so, but they will exhibit a reflex twitch in the fore-arm which can be recognised with the hand, most marked on the inside and front where the lesion is in that position in the foot, and on the outside and back when the lesion is in a corresponding position in the foot.

Another useful aid to diagnosis is to attach a block of hard wood to a piece of hoop iron, which can be inserted under the shoe, before trotting. This is especially useful in the diagnosis of navicular disease.

Walking or trotting over loose stones or gravel helps one greatly in cases of tender and thin sole, pedal ostitis and corn.

What Can We Do When a Diagnosis is Made?

Shoulder cases.—I am a firm believer in the intra-muscular injection of turpentine. I do not place much faith in superficial applications. As a rule and given time, injured nerves will regenerate if the sheath is intact. Muscle wasting needs active or drastice therapeutic measures, and I know of nothing better than turpentine to hasten resolution. In tendon and joint troubles, and where it can be satisfactorily applied, I favour Scotts dressing, i.e., Ung. Hyd. Co. applied under oiled silk and replaced every second or third day. There is no doubt that diet plays a part and cod liver oil internally is valuable in promoting resolution. I am also, in spite of modern ideas, a firm believer in the value of the firing iron in suitable cases. There are many horses performing well to-day who, but for the firing iron, would have been cat's meat. In the chronic foot case much can be done by suitable shoeing and judicious trimming, almost manicuring, of the hoof. In this way we can exert some control over physiological function and anatomical form. For example, if you shorten the toe and alter its angle the quarters will strengthen and the heels deepen and widen. A dropped sole will tend to rise under the same measures.

Hoof section is useful; it has the immediate effect of relieving pressure and by allowing of the elastic opening and closing of the hoof it establishes the pump-like action so essential to an efficient circulation. I have always been interested in this "manicuring" of the hoof and surgical shoeing, and I contend that 50 per cent. of horses lame in the foot can be restored by these means alone. I have seen a well-known Arab (native) dealer restore old fevered dropped soled feet in this manner to normality.

To finish, I would draw your attention to a method which gives relief in many cases of navicular disease.

The hoof is prepared with the toe shortened and rasped off so that it is set at an angle of about 120 deg. The shoe has a bent toe, no toe clip and the branches are narrow and gradually deepen towards the heel. The idea is to prevent the hitting of the toe and to let the wall bear all the weight and to put the frog out of action.

When the shoeing is completed I put the horse to graduated exercise or work. It works best on road horses, but I have seen gratifying results in hunters and in one very special show jumper. "Hitchins" rubber heel pads may be combined with the above shoe, with advantage.

I close these remarks with the hope that I have opened a flood of discussion. Our forebears undoubtedly did know a lot about horses. My fear is that for want of interest such knowledge will be lost. We must keep alive the cult of the horse and try to add to the store of knowledge.

ABSTRACT

SOME OBSERVATIONS ON EQUINE PRACTICE AND ITS RELATION TO THE BREEDING OF THOROUGHBRED MARES

By MAJOR R. C. CROWHURST, M.R.C.V.S., and WILLIAM CASLICK, D.V.M.

N.A.V., 27, 1946, 12, 761-767.

In a paper delivered at the joint meeting of the Southern Veterinary Medical Association and the Kentucky Veterinary Medical Association at Louisville, the authors reviewed:

(1) Ovulation and time of breeding in the mare.

(2) Anœstrous mares.

(3) Infections of the genital tract of the mare.

The paper was based primarily on their own observations but many other authorities are quoted.

(1) *Ovulation and time of breeding*: The only constant finding regarding the œstrual cycle is its irregularity. The duration of œstrus covers a very wide range, the greatest being from 7 to 107 days. On average, however, the accepted duration period of 21 days is correct in the normal mare. The average di-œstrous period is from 15-16 days. Œstrum also varies in its duration and the authors quote Hammond (7 days) and Andrews and McKenzie (5½ days). They also quote Caslick (1 to 103 days). No doubt the latter range included some abnormal mares. Œstrum tends to last longer in the early part of the breeding season, particularly in maiden mares and in old mares in poor condition.

Ovulation most frequently occurs towards the end of the œstrual period. It occurs rarely after the end of the period.

Mares must be bred before ovulation occurs. It takes 5-8 hours for the sperm to reach the Fallopian tube, and virile sperms should be at the upper end of the tube when ovulation occurs in order for fertilisation of the ovum to occur. There is apparently great variation of opinion as to the day of breeding in relation to the onset of œstrum. To the breeder, the onset of œstrum is his only guide. After reviewing the opinions of the various authorities, the authors recommend:

(a) Mares going to healthy and fertile stallions should be bred on the second or third day from onset of œstrum.

(b) Second service on the second day after first service should be discontinued. It is wasteful and not really necessary.

(c) Mares should be teased daily or every other day. If they remain well in œstrum on the fourth day following the first service, they should be re-bred that day.

(2) *Anœstrous mares*: The authors say that the causes of anœstrum in the mare is not well understood. They list some of the known causes:—

(a) Silent heat. Ovaries produce ripe follicle with ovulation but the mare fails to show physiological œstrum. Probably the most common cause of anœstrum. The mares do not react to the teaser. It is most often noted in mares suckling foals.

(b) A sub-functioning of the endocrine system in general and a resulting lack of stimulation of the ovary to produce ripe follicles.

(c) Cystic ovaries.

(d) Persistent Copus luteum.

(e) Early abortion, usually unobserved. There may be resorption of fœtus.

They now quote Caslick's records for a period of 7 years, counting all mares that went 45 days or more without showing heat periods and were not pregnant. Excluding 17 cases of suspected fœtal abortion, there were 97 anœstrous mares out of 1,882 mares; 57 cases were in foaling mares, 30 in barren mares. Of the 97 anœstrous mares, 79 (81.4 per cent.) came back in œstrum of their own accord without stimulation in time to breed before the end of the season, and of them 45 (46.4 per cent.) became pregnant; 40.35 per cent. of the foaling mares, 50 per cent. of the barren mares, and 70 per cent. of the maiden mares.

The authors have used stilbœstrol on a limited number of anœstrual mares. "If the genital tract of the mare shows some evidence of an approaching œstrus period, then one injection of stilbœstrol will usually induce immediate psychological œstrum, followed in some cases by a normal œstrual cycle. If, however, at the time of injection the genital tract is in a state of complete anœstrum, an immediate response cannot be expected."

Fourteen mares are quoted, and pregnancy followed the use of stilbœstrol in 50 per cent., compared with 46.96 per cent. in untreated mares.

(3) *Infection of the genital tract*: The symptoms shown are those of vaginitis cervicitis and for endometritis. Very rarely does a clinically infected mare become pregnant and produce a normal, healthy foal at full term. Infections of the genital tract are probably the second greatest cause of infertility in T.B. mares.

Infecting organisms gain entrance via the vagina, and the greatest predisposing cause is the condition known as wind sucking. In wind sucking there is an impaired function of the external parts of the genital tract. When the walls of the vulva and vagina do not come together, contaminated air and even fæces may enter and infection result. The condition may be met with in any type of mare, even yearlings, and from a variety of causes.

A modified Colporrhaphy operation is recommended. It does not lead to the cure of all cases of infection.

It is interesting to note, however, that W. Caslick performed this operation on 36 mares. All these mares showed varying degrees of infection and evidence of wind sucking. Thirteen were grossly infected. Of these 36 mares, 22 (61 per cent.) became pregnant that season. No other treatment was given.

NEWS

ROYAL VETERINARY COLLEGE AND HOSPITAL

Annual Report for the Academic Year ended September, 30, 1946

We have very much regret in reporting the death of the Right Honourable Lord Mildmay of Flete, P.C., who was a Vice-President of the College for ten years.

Teaching

During the session 103 new students were admitted, as compared with 83 in the session 1944-45; in addition, 27 students returned from the Forces, making a total of 130. The total number of students at the beginning of the session was 370, the number for the previous year being 317.

At the examinations held by the Royal College of Veterinary Surgeons in December, 1945, 111 students presented themselves for examination and 77, or 69 per cent. passed; and at the examinations held in July, 1946, 310 students presented themselves and 221, or 71 per cent., passed. The percentage of passes in December, 1944, and July, 1945, were 68 per cent. and 79 per cent. respectively.

During the year under report 60 students obtained the Diploma of Membership of the Royal College of Veterinary Surgeons, as compared with 39 who qualified in the previous year.

The number of students preparing for the B.Sc. (Veterinary Science) degree in October, 1945, was 84 enrolled in all years, compared with 91 in 1944, 76 in 1943, 68 in 1942, 58 in 1941 and 43 in 1940.

Research

A—In the College

Department of Surgery and Obstetrics.—Investigations have been made into the value of a specially constructed metal detector for the detection of metallic foreign bodies in cattle and other animals. Preliminary observations indicate that it is of value in clinical medicine and surgery.

An electric stethoscope, consisting of stethophone, amplifier and loud-speaker, has been devised. Its application to clinical teaching, especially in the diagnosis and demonstration of respiratory and cardiac diseases, is being developed.

The condition known as "night-blindness" in the Red Setter is being investigated.

Department of Anatomy.—Research into the cardio-vascular and respiratory systems of the horse has been initiated in collaboration with the Department of Physiology.

Division of Histology and Embryology.—Work on the problems of fertilisation and the effects of X-irradiation has been continued.

Investigation is being made of the source of the hormone in pregnant mares' serum.

Other studies include "Fœtal Anasarca," the clotting properties of fœtal blood and the permeability of the placenta.

Department of Physiology.—The studies on circulation have been continued, with special reference to peripheral circulation.

The work on the nervous control of respiration is being continued.

B—In the Research Institute of Animal Pathology

The properties of Corynebacterium renale and a study of the value of some therapeutic agents in C. renale infections in laboratory animals.

A study of the incidence of losses amongst calves and of the natural circumstances under which such losses occur.

Further studies of the pathogenesis of Johne's disease.

Sheep abortion and the study of the antigenic structure of numerous strains of Vibrio fœtus.

The pathology and bacteriology of calf pneumonia.

A survey of the normal agglutinins in the sera of cattle against actinobacillus.

The study of the pathology of perosis in chicks has been continued.

Further study of the toxicity of fractions of ricin and the preparation of antitoxin and the anti-agglutinin factor, in collaboration with the Division of Chemistry.

Further investigation of the life-cycle of Babesia bovis in the tick.

Study of an unusual species of œsophagostome recovered from a Père David's deer.

The Hospital

At the Beaumont Animals' Hospital, attendances at the clinic numbered 16,708, compared with 14,137 during the preceding year. The number of animals seen during the last quarter of the year, 5,036, was the highest for any quarter of any previous year.

Staff

Appointments

H. W. J. Adams, B.A., Secretary and Bursar.

P. M. Bennett, M.R.C.V.S., Demonstrator Anatomy.

C. A. E. Briggs, M.R.C.V.S., Demonstrator Pathology.

C. B. Hart, M.R.C.V.S., House Surgeon, Wallingford Practice.

E. W. Jones, M.R.C.V.S., Demonstrator Surgery.

E. F. Lewis. M.R.C.V.S., Surgeon-in-Charge, Steyning Practice.

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E. G. White, Ph.D., Reader Pathology.

Mrs. J. G. Wright, M.R.C.V.S., House Surgeon, Beaumont Animals' Hospital.

Finance

The accounts for the year 1945-46 presented herewith show that expenditure exceeded income, excluding Government grant, by £47,177, as compared with £23,004 in the preceding year. Revenue expenditure was £67,576, against £46,346 for 1944-45, and the increase is spread over all items. In October, 1945, the teaching of first and second year students was resumed in London, and the greater part of the Camden Town buildings became occupied. Establishment and maintenance charges were thus increased, and expenditure under these headings will show a further expansion in the year 1946-47 owing to the resumption of the teaching of third year students in London in October, 1946. The work of

rehabilitation continued during 1945-46, and expenditure under this heading will go on until full rehabilitation is accomplished. Some expenditure on the West Grinstead Park Estate followed the beginning of the lease on September 29, 1945.

Income, excluding Government grant, was £20,399 for 1945-46, compared with £20,343 for the preceding year. Income from requisitioned premises fell by £2,863, but that from other sources rose by £2,919, of which £2,324 was attributable to increase of income from students' fees. Donations increased by £268, while subscriptions were virtually unchanged.

The net cost of the Beaumont Animals' Hospital was £2,090, compared with £1,298 for 1944-45, the increase being due mainly to higher establishment expenses.

This report of the oldest teaching institution in this country will assure the reader that the R.V.C. has lost none of its vigour in its 156 years of existence. It is good to note that Government recognition and support is on a more substantial scale than in the past. The great numbers of students may give concern to many.

EDITOR.

CALF SALVAGING SCHEME*

IN the spring of last year the Livestock Improvement Sub-Committee of the Breconshire War Agricultural Executive Committee realised that many hundreds of good Hereford and Hereford crossbread calves were going for slaughter prematurely through the Ministry of Food's Collecting Centres. So a scheme was put into operation on April 1 whereby the Animal Husbandry Officers attend the principal markets in the county and salvage the best type of calf.

The calves are taken to the Committee's Collecting Centre at Aberyscir Farm. They are immediately inoculated against white scour, and the loss is as low as 1 per cent. The calves remain at Aberyscir only for such time as a load of 20 to 30 can be collected for export to English counties. The method of rearing that has been successfully practised is quite simple but requires great skill on the part of the stockman, since the number of calves varies from week to week, depending on the demand from importing counties. The usual practice, however, is for the newly calved nurse cows to suckle for about eight weeks, after which they weaned; and a further three calves are suckled for a similar period, followed by two calves. The cows are usually able to suckle one more calf, depending, of course, on her milking capacity. The cows used for this job are those unsuited for the dairy herd; they are kept for three or four seasons and are always mated to a Hereford bull, usually producing a calf every 14 months or so.

Young calves are encouraged to eat concentrates at a very early age, and clean water is provided *ad lib.* Only the best quality hay is fed.

* Ministry of Agriculture News Service, No. 396, April 21, 1947.

To date about 700 calves have been salvaged. Taking the average live weight of a beast to be 10 cwt. at 2½ years old, it is seen that about 200 tons of beef will be made available for the nation.

The demand for good quality beef calves far exceeds the supply, counties like Gloucester, Northampton and Norfolk taking most of the animals.

REVIEW

The Circulation in the Fœtus (a synopsis for students). By K. J. FRANKLIN, D.M., F.R.C.P., A. E. BARCLAY, O.B.E., D.M., F.R.C.P., F.F.R., F.A.C.R., and MARJORIE M. L. PRICHARD, M.A., Nuffield Institute, Oxford. Price: 2s. 6d. Oxford: Blackwell Scientific Publications, Ltd.

THIS synopsis of an extensive account of the fœtal circulation published in 1944 was produced by the authors on behalf of students and others who, while desiring an accurate knowledge of the fundamentals of the subject, have not the time to read through the detailed literature.

Although it is essential to know the basic anatomical facts when reading this book, it gives, in its eleven-page account, a very good idea of the changes taking place in the fœtal circulatory system at the time of parturition. It is rendered more interesting by a description of experimental detail carried out on the pregnant ewe.

The latter part of the book consists of several radiographs and diagrams accompanied by explanatory notes, which greatly assist in impressing on the reader all those points which are stated in the first few pages.

P.M.B.

OMISSION

IN the article by L. M. Markson which appeared in the May, 1947, issue, the legends for figures on the first plate, left to right (1) and (2) and bottom (3), are as follow:

Plate 1.—Hæmosiderin in obliterated vasa vasorum of an affected artery. Hæmatoxylin and eosin. x 70.

Plate 2.—Fibrosis of the entire vascular wall with great extension of the adventitia. Kidney. Azan. x 75.

Plate 3.—Obliterated vessel with its elastic interna completely destroyed. Hart's Stain. x 200.

Second plate, top and bottom (4) and (5) legends read as follow:

Plate 4.—Chronic endarteritis and fibrosed media. Hart's Stain. x 75.

Plate 5.—Large mass of mainly collagenous fibrous tissue. Complete obliteration of the vessels and only a few strands of elastic fibrous tissue visible. Hart's Stain (case 2). x 200.

ERRATA

In the article by W. M. Allcroft which appeared in the May, 1947, issue, the legends to Figs. 3 and 4 should have read as follows:

Fig. 3.—Behaviour of blood constituents after separate intravenous injections of (*a*) calcium gluconate equivalent to 7.33 g. Ca, and (*b*) magnesium sulphate equivalent to 1.8 g. Mg in a 1,000 lb. bovine.

Fig. 4.—Behaviour of blood constituents after intravenous injection of 75 g. magnesium sulphate in 300 ml. water in a 1,000 lb. bovine.

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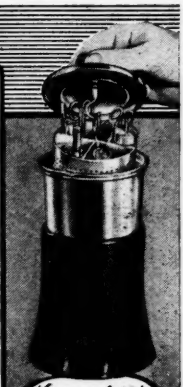

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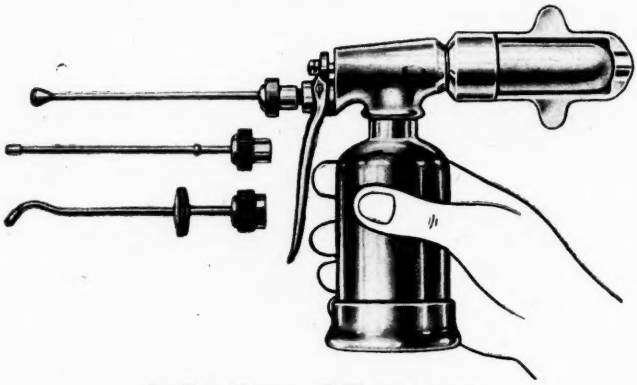

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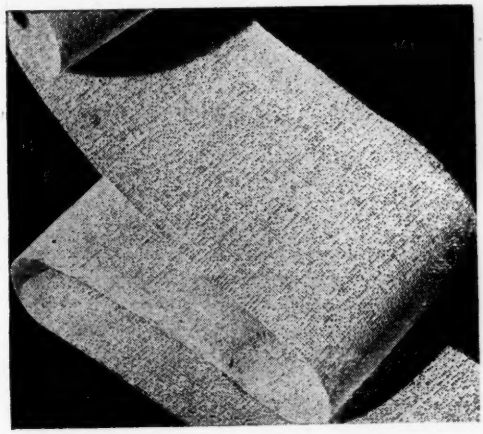

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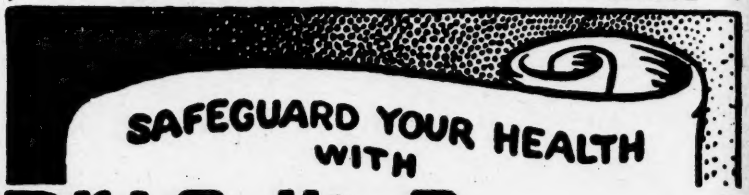

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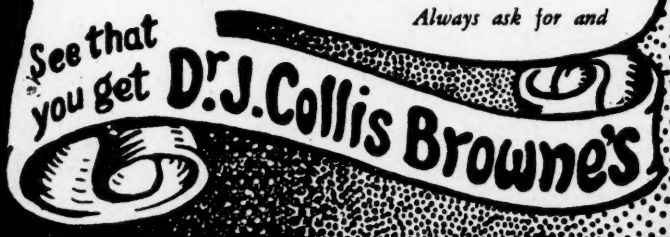

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